## REMARKS/ARGUMENTS

In the Advisory Action mailed August 30, 2007, the Examiner informs Applicants that the amendment filed on August 07, 2007 was not entered. The Examiner alleges that the amendments did not place the application in better form for allowance. Specifically, the Examiner alleges, based on Schemes 1-3 on pages 98-101, no support for L is less than 2 carbons can be found and no terminal disclaimer was filed.

In response, and because Applicants are unsure whether the Examiner has considered the Remarks/Arguments made in the amendment filed on August 7, Applicants address issues that were raised in both the Examiner's Final Office Action and Advisory Action.

(1)

Applicants note with appreciation that the Examiner has entered the amendment and response filed on March 15, 2007.

Applicants cancel claims 174-175. Claims 109-116, 118-128, 130-140, 143-173, and 176-177 are pending.

(2)

Applicants note with appreciation that the Examiner has withdrawn the rejection of claims 109, 111, 112, 117, 119, 121, 122-124, 129, 131, 133-136, 141 and 143 under 35 U.S.C. § 112, Second Paragraph for the term "comprising" in view of the amendment.

(3)

## a) "M" and "E or Z"

Applicants note with appreciation that the Examiner has withdrawn the rejection of claims 109, 112, 121, 124, 133 and 136 under 35 U.S.C. § 112, Second Paragraph for the scope of "M" and for "E or Z" in view of the amendments.

## b) "substituent that is convertible in vivo to hydrogen"

The Examiner rejected claims 109, 121, and 133 based on new matter for the insertion of "or a substituent that is convertible *in vivo* to hydrogen" into the definition of  $R_{14}$  in claims 109, 121 and 133. The Examiner also rejected claims 112, 124 and 136 for not explicitly naming the members of claims 109, 121, and 133, respectively, that can be converted to hydrogen *in vivo*.

Applicants amend claims 109, 121, and 133 to remove the recitation and respectfully request the Examiner to withdraw the rejections of the claims based on new matter.

Applicants amend claims 112, 124 and 136 to remove "substituent that is convertible in vivo to hydrogen" from the definition of  $R_{14}$ .

As a result of the amendments, claims 112, 124 and 136 properly depend from claims 109, 121 and 133, respectively and the scope of  $R_{14}$  is clear. Accordingly, this rejection may be withdrawn. Applicants reserve the rights to pursue other members of  $R_{14}$  in claims 109, 121 and 133 as originally filed that can be converted to hydrogen *in vivo* in later filed applications.

(4)

The Examiner maintains the rejection of claims 109 and 121 under 35 U.S.C. § 112, First Paragraph, for allegedly failing to comply with the enablement requirement for the scope of L other than C2-C10. Applicants provided examples in Applicants' Exhibits A-D in response to the previous office action that people skilled in the art would have known to select the linker among those available. The Examiner alleges that none of the recited material indicates any biological activity nor any support of an art recognized Markush variation as the exemplified C2-C10 compounds as histone deacetylase inhibiting activity. The Examiner asserts that the mere provision of the "language" does not constitute enablement.

Applicants disagree with the Examiner's assessment of the examples previously provided by Applicants. Applicants also disagree with the Examiner's assessment of the synthesis scheme. However, in the interest of advancing prosecution of the present application, Applicants amend claims 109 and 121 to limit the atoms of L to carbon atoms. Applicants believe the amendment overcomes the rejection of claims 109 and 121 under 35 U.S.C. § 112, First Paragraph, and respectfully request the Examiner to withdraw the rejection.

Patent HDAC-5005-C2

(5)

Applicants note with appreciation that the Examiner has withdrawn the rejection of claims 109-112, 115, 121-124 under 35 U.S.C. §103(a) as being unpatentable over Vourloumis et al. Tetrahedron Lett. ("Vourloumis") in view of CA139:133505.

(6)

The Examiner provisionally rejects claims 109-116, 118-128, 130-140, 143, and 144-177 on the ground of non-statutory obviousness-type double patenting as being unpatentable over the pending claims of co-pending Application No. 10/803,575. Applicants submit herewith a terminal disclaimer which obviates the rejection; accordingly, Applicants respectfully request the Examiner to withdraw the rejection on the ground of non-statutory obviousness-type double patenting over co-pending Application No. 10/803,575.

## CONCLUSION

Applicants earnestly believe that they are entitled to letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Dated: October 9, 2007

Customer No. 32793 Takeda San Diego, Inc. 10410 Science Center Drive San Diego, CA 92121

Telephone: (858) 622-8528 Facsimile: (858) 550-0992